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| 09/972,268 | 10/05/2001 | Peter R. Baum | 3101-A | 4855 |

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| EXAMINER |
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| ART UNIT | PAPER NUMBER |
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| 1644 | |

DATE MAILED: 10/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/972,268 | BAUM ET AL. | |
| | Examiner | Art Unit | |
| | Maher M. Haddad | 1644 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *30 June 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *59-111* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *59-111* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 6/30/03, is acknowledged.

2. Claims 59-111 are pending and under consideration.

3. Applicant's IDS, filed 6/30/03, is acknowledged, however, reference No. 1B is crossed out as the English translation of the entire document was not found. Applicant is invited to produce such documents. Applicant submits that the EP 1 179 592A and US2003/0008334 A1 publications (filed on 6/30/03) each appear to be an English translation of the WO 01/66736 publication. However, the Examiner does not read Japanese, thus in order to consider the WO 01/66736, it has to be translated to English. The Examiner initials the US2003/0008334 A1 publication.

4. The declaration by Peter R. Baum, William C. Fanslow III, Timothy E. Lofton, Eric A. Sorensen and Adel Youakim, under 37 CFR 1.131 filed 6/30/03 to antedate Reymond et al and Satoh-Horikawa et al, references is sufficient to overcome the rejection based upon 35 U.S.C. § 102(a) and 35 U.S.C. 103 as obvious in light of the combination of the Reymond et al or Satoh-Horikawa et al references in view of the `520 or `371 patents.

5. The amendment filed 6/30/03 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

The amendment filed on 6/30/03 to the paragraph beginning at page 6, line 15 and to replace Table beginning at page 7, line 7 to correct typographical errors in Table 2 and to more clearly set forth the information contained in the table represents a departure from the specification and the claims as originally filed. However, the specification and the claims as originally filed have no support for the new consensus replacement of Table 2 and the new insert at page 6, line 15 paragraph. It is noted that Table 2 as originally filed shows a consensus sequence identical among at least majority of amino acid sequences in the alignment.

Applicant is required to cancel the new matter in the response to this Office action.

6. Applicant's cancellation of Claims 1-11, 19 and 54-58 filed 6/30/03 have obviated the previous objections and rejections with respect to Claims 1-11, 19 and 54-58.

7. The following New Grounds of Rejections are necessitated by the amendment submitted 6/30/03.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

*The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.*

9. Claims 60, 67, 73-78, and 105 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter rejection.

The phrases:

A. "extending from amino acid 58 through the C-terminus of SEQ ID NO:4, 6, 13 or 15" claimed in claim 60(a-c), lines 3-8,
B. "extending from amino acid 58 through the C-terminus of SEQ ID NO:10, 12, 14, 16 or 31" claimed in claim 67(a-d), lines 3-11,
C. "amino acids 58 through 342 of SEQ ID NO 31" claimed in claim 73(a), line 3,
D. "amino acids 74 through 342 of SEQ ID NO:31" claimed in claim 73(b), line 4,
E. "amino acids 74 through 365 of SEQ ID NO:31" claimed in claim 73(d), line 6,
F. "amino acids 58 through 342 of SEQ ID NO:31" in claim 105(a), line 3,
G. "amino acids 74 through 342 of SEQ ID NO:31" in claim 105(c), line 5,
H. "amino acids 58 through 365 of SEQ ID NO:31" in claim 105(e), line 7, and
I. "amino acids 74 through 365 of SEQ ID NO:31" in claim 105(f), line 8

represent a departure from the specification and the claims as originally filed.

Applicant's amendment filed 6/30/03 points to the specification at pages 1-3, 5, 13-15, 18, 19-20, 21-22 and 31 for support for the newly added limitations of A-I above. However, the specification does not provide a clear support for these limitations. The instant claims now recite limitations which were not clearly disclosed in the specification and recited in the claims as originally filed.

10. Claims 59-111 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a substantially purified polypeptide comprising an amino acid of SEQ ID NO: 2, 4, 6, 8, 10, 12 and 31, wherein SEQ ID NO:4, 6, 10, 12, and 31 comprising amino acids 74-152, 189 to 250 and 287 to 342, and SEQ ID NO: 13-16, wherein the polypeptide consists of amino acid sequence that binds to nectin-1 for inhibiting endothelial cell migration; does not reasonably provide enablement for any substantially purified polypeptide comprising amino acids 58-404 of SEQ ID NO:4 or 6, in claim 59, wherein said polypeptide comprises any amino acid sequence extending from amino acid 58 through the C-terminus of SEQ ID NO:2 or 6, 13, 15 in claim 60; Any substantially purified polypeptide comprising amino acids 74 through

635 of SEQ ID NO: 10, 12 or 31 in claim 66, wherein said polypeptide comprises any amino acid sequence extending from amino acid 58 through the C-terminus of SEQ ID NOs:10, 12, 14, 16, or 31 in claim 67; any substantially purified polypeptide comprising any amino acid sequence selected from the group consisting of amino acids 58-342 of SEQ ID NO:4, 6, 10, or 31, amino acids 74-342 of SEQ ID NO:4, 6, 10, 12 or 31, amino acids 74-342 of SEQ ID NO:4, or 6 and amino acids 74-365 of SEQ ID NO:10, 12, or 31 in claim 73; any substantially purified polypeptide comprising any amino acid sequence that inhibits endothelial cell migration and that shares at least 80% amion acid identity across the length of amino acids 58-404 of SEQ ID NO:4 or 6 in clai 79, wherein said polypeptide comprises an amino acid sequence sharing 85%, 90%, 95% or 99% amino acid identity across the length of amino acids 58 through 404 of SEQ ID NO: 4 or 6 in claim 80; any substantially purified polypeptide comprising an amino acid sequence that inhibits endothelial cell migration and that shares at least 80% amino acid identity across the length of amino acids 74 through 365 of SEQ ID NO:10, 12 or 31 in claim 86, wherein said polypeptide comprises an amino acid sequence sharing 85%, 90%, 95%, or 99% amino acid identity across the length of amino acids 74 through 365 of SEQ ID NO:10, 12 or 31 in claim 87; any substantially purified polypeptide comprising an amino acid sequence that inhibits endothelial cell migration and that shares at least 80% amino acid identity across the length of a contiguous amino acid sequence comprising amino acids 74 through 152 and 189 through 250 of SEQ ID NO:4, 6, 10, 12 or 31 in claim 93, wherein said polypeptide comprises an amino acid sequence sharing 85%, 90%, 95% or 99% amino acid identity across the length of a contiguous amino acid sequence comprising amino acids 74 through 152 and 189 through 250 of SEQ ID NO:4, 6, 10, 12, or 31 in claim 94; any isolated polypeptide of claim 93 produced by a process comprising (a) culturing a recombinant host cell comprising any "polynucleotide" having nucleotide sequence encoding said polypeptide and (b) isolating said polypeptide in claim 100, wherein said polypeptide is produced by a process comprising culturing a recombinant host cell comprising a polynucleotide having a nucleotide sequence encoding said polypeptide or The polypeptide of claim 100, wherein said polypeptide is produced by a process comprising culturing a recombinant host cell comprising any polynucleotide having any nucleotide sequence encoding said polypeptide, wherein said nucleotide sequence is selected from the group consisting of nucleotide4s 172-1026 of SEQ ID NO:3, 5, 9 or 11; nucleotides 172-1212 of SEQ ID NO:3 or 5, and nucleotides 172-1098 of SEQ ID NO: 9 or 11 in claim 102; wherein said polypeptide comprises an amino acid sequence selected from the group consisting of (a) amino acids 58-342 of SEQ ID NO: 4, 6, 10, 12 or 31, (a) amino acids 58-404 of SEQ ID NO:4 or 6, (c) amino acids 74-342 of SEQ ID NO:4, 6, 10, 12 or 31, (d) amino acids 74-404 of SEQ ID NO:4 or 6, (e) amino acids 58 through 365 of SEQ ID NO:10, 12, or 31 and (f) amino acids 74-365 of SEQ ID NO:10, 12 or 31 in claim 105, wherein said polypeptide is produced by a process comprising culturing a recombinant host cell into which a polynucleotide comprising a nucleotide sequence encoding said polypeptide has been introduced in claim 111. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims for the same reasons set forth in the previous Office Action, mailed 12/31/02.

Applicant's arguments, filed 6/30/03, have been fully considered, but have not been found convincing.

Applicant argues under teaching of essential sequences subtitle, that the specification provides teaching to those of skill in the art that the portion of the nectin-3 polypeptides involved in inhibition of endothelial cell migration includes the Ig domains of the extracellular region. Applicant further argues that a purported lack of teaching of regions related to biological function is not an adequate basis upon which to reject the claims.

The claims as written encompass a broad genus of polypeptides with an unlimited number of possibilities with regard to the length of the polypeptide sequence. Further, the enablement issues of making the protein still remain because the specification does not teach and provide sufficient guidance as to which amino acid of the 74-152, 189-250 and 287-342 of SEQ ID NO:4, 6, 10, 12 or 31( for example) would have been altered such that the resultant polypeptide would have retained the function of inhibiting endothelial cell migration. In addition, variation up to 20% of amino acids 74-152 ($79 \times 19^{20}$), amino acids 189-250 ($62 \times 19^{20}$) and amino acids 287-342 ($56 \times 19^{20}$) provide a range of activities, not all which are necessarily predictive of inhibiting endothelial cell migration. Furthermore, the team "comprising" in claims 59-60, 66-67, 73, 79-80, 86-87, 93-94 and 105 is open ended, which opens the claim to include additional unrecited amino acids on either or both of the N- or C- termini of a given sequence. Therefore, absent the ability to predict which of these polypeptides would function as claimed for one of skill in the art to practice the invention as claimed would require a level of experimentation that is excessive and undue.

Applicant argues under teaching of functional variants subtitle, that the specification clearly teaches that certain variants of the nectin-3 polypeptide sequences of SEQ ID NO:2, 4, 6, 10, 12, or 31 would be expected by those of skill in the art to be functional. Applicant points to the specification at page 6, lines 22-33 to support that the specification provides clear guidance to those of skill in the art.

While the Examiner acknowledge that table 2 and the specification on page 6, lines 22-33 provide some guidance for functional variants, however, it is recognized in the prior art that the function of a protein depends on the sequence of its amino acids in a certain pattern, conformation of the protein due to the amino acid sequence and the functional properties of the different parts of the protein. Further, the specification does not teach which amino acid outside the 58-404, 74-365, 58-342, 74-342, 74-404, 74-365, 58-C-terminus or 74 through 152, 189-250, and 287-342 of SEQ ID NO:2, 4, 6, 10, 12 or 31 core structure would not alter all the activities of the claimed polypeptide. Therefore, the specification fails to provide sufficient guidance as to which amino acid of SEQ ID NO: 2, 4, 6, 10, 12 or 31 is essential for maintain its biological activity of amino acid 74-152 of SEQ ID NO:2, 4, 6, 10, 12 or 31.

Applicant further argues that Attwood and Skolnik and Fetrow references are not applicable to the disclosure of Applicants, in which functional data regarding the polypeptide sequences is presented. Further the issues that the Attwood and Skolnik and Fetrow references raise as being of concern to database annotators, are either not relevant to the nectin-3 polypeptides of the invention or have been addressed by the disclosure of the specification. Applicant provides an

Example that Attwood caustion against making a prediction of biological function on the basis of sequence similarity to only one of several functional modules or domains in a protein. Applicant asserts that this hypothetical concern is not applicable to the enablement of the claimed subject matter, because there is description in the specification of the overall similarity of the structure of nectin-3 polypeptides with other nectin polypeptides: the three Ig domains, the transmembrane domain, and the similarity of sequences at the intracellular C-terminus that are seen in the members of the nectin polypeptide family.

However, Skolnick et al. (Trends in Biotech. 2000; 18(1):34-39) state that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the specific details of protein function. Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2). Therefore, even though the overall similarity of the structure of nectin-3 polypeptides with other nectin polypeptides: the three Ig domains, the transmembrane domain, and the similarity of sequences at the intracellular C-terminus that are seen in the members of the nectin polypeptide family only experimental research can confirm the artisan's best guess as the function of the structural related protein.

Regarding Metzler et al, Applicant argues that the Office action fails to mention a critical fact about the amino acids that were mutated in the Metzler et al reference. Applicant indicated that all of the mutations were made in residues that were highly conserved in CTLA4 family polypeptides and would therefore be expected, based on the teaching at page 6 of the specification to frequently result in changes in biological function. Applicant concluded that this reference cannot be cited for the proposition that any of a variety of single amino acid differences can alter or abolish biological activity. Applicant contended that Metzler et al provides experimental evidence in support of the teaching of the specification namely, that changes to conserved residues are likely to change the biological activity of a polypeptide.

Metzler et al reference demonstrates that event a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein. Further, Martinez et al in J. Virology 75(22):11185-11195, 2001, have identified two regions and specific amino acid residues within the V domain of nectin-2 that are critical for HSV entry activity. Martinez et al teach that while replacement of amino acids in region A or B of mouse nectin-2 with human nectin-2 sequences conferred normal or enhanced entry activity. However, replacement of amino acid in region B of human nectin-2 with the corresponding mouse amino acid (M89F) eliminated all HSV entry activities, even though region A was unchanged (see page 11192, 2$^{nd}$ col., 4$^{th}$ paragraph). Thus it is unpredictable if any functional activity will be shared by two polypeptides having less than 100% identity over the full length of their sequences.

Applicant submits that testable function has not been set forth clearly enough to be an adequate basis for rejection of the claims. However, claiming polypeptides by function only fails to enable the skilled artisan to make and use the scope of such "polypeptides", as there is

insufficient guidance and direction as to structure of the polypeptides, broadly encompassed by the claimed invention. "It is not sufficient to define the recombinant molecule by its principal biological activity. e.g. having protein A activity, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property" Colbert v. Lofdahl, 21 USPQ2d, 1068, 1071 (BPAI 1992).

Consequently, without additional guidance in the specification, and the dearth of information in the art, for one of skill in the art to practice the invention as claimed, would require experimentation that is excessive and undue. The amount of guidance or direction needed to enable an invention is inversely related to the mount of knowledge in the state of the art as well as the predictability in the art (In re Fisher, 427 F.2d 833, 839, 166 USPQ 18,24 (CCPA 1970)).

11. Claims 59-111 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the same reasons set forth in the previous Office Action, mailed 12/31/02.

Applicant is in possession of a substantially purified polypeptide comprising an amino acid of SEQ ID NO: 2, 4, 6, 8, 10, 12 and 31, wherein SEQ ID NO:4, 6, 10, 12, and 31 comprising amino acids 74-152, 189 to 250 and 287 to 342, and SEQ ID NO:13-16 wherein the polypeptide consists of amino acid sequence that binds to nectin-1 for inhibiting endothelial cell migration.

Applicant is not in possession of any substantially purified polypeptide comprising amino acids 58-404 of SEQ ID NO:4 or 6, in claim 59, wherein said polypeptide comprises any amino acid sequence extending from amino acid 58 through the C-terminus of SEQ ID NO:2 or 6, 13, 15 in claim 60; Any substantially purified polypeptide comprising amino acids 74 through 635 of SEQ ID NO: 10, 12 or 31 in claim 66, wherein said polypeptide comprises any amino acid sequence extending from amino acid 58 through the C-terminus of SEQ ID NOs:10, 12, 14, 16, or 31 in claim 67; any substantially purified polypeptide comprising any amino acid sequence selected from the group consisting of amino acids 58-342 of SEQ ID NO:4, 6, 10, or 31, amino acids 74-342 of SEQ ID NO:4, 6, 10, 12 or 31, amino acids 74-342 of SEQ ID NO:4, or 6 and amino acids 74-365 of SEQ ID NO:10, 12, or 31 in claim 73; any substantially purified polypeptide comprising any amino acid sequence that inhibits endothelial cell migration and that shares at least 80% amion acid identity across the length of amino acids 58-404 of SEQ ID NO:4 or 6 in clai 79, wherein said polypeptide comprises an amino acid sequence sharing 85%, 90%, 95% or 99% amino acid identity across the length of amino acids 58 through 404 of SEQ ID NO: 4 or 6 in claim 80; any substantially purified polypeptide comprising an amino acid sequence that inhibits endothelial cell migration and that shares at least 80% amino acid identity across the length of amino acids 74 through 365 of SEQ ID NO:10, 12 or 31 in claim 86, wherein said polypeptide comprises an amino acid sequence sharing 85%, 90%, 95%, or 99% amino acid identity across the length of amino acids 74 through 365 of SEQ ID NO:10, 12 or 31 in claim 87; any substantially purified polypeptide comprising an amino acid sequence that inhibits endothelial cell migration and that shares at least 80% amino acid identity across the length of a contiguous amino acid sequence comprising amino acids 74 through 152 and 189 through 250 of

SEQ ID NO:4, 6, 10, 12 or 31 in claim 93, wherein said polypeptide comprises an amino acid sequence sharing 85%, 90%, 95% or 99% amino acid identity across the length of a contiguous amino acid sequence comprising amino acids 74 through 152 and 189 through 250 of SEQ ID NO:4, 6, 10, 12, or 31 in claim 94; any isolated polypeptide of claim 93 produced by a process comprising (a) culturing a recombinant host cell comprising any "polynucleotide" having nucleotide sequence encoding said polypeptide and (b) isolating said polypeptide in claim 100, wherein said polypeptide is produced by a process comprising culturing a recombinant host cell comprising a polynucleotide having a nucleotide sequence encoding said polypeptide or The polypeptide of claim 100, wherein said polypeptide is produced by a process comprising culturing a recombinant host cell comprising any polynucleotide having any nucleotide sequence encoding said polypeptide, wherein said nucleotide sequence is selected from the group consisting of nucleotide4s 172-1026 of SEQ ID NO:3, 5, 9 or 11; nucleotides 172-1212 of SEQ ID NO:3 or 5, and nucleotides 172-1098 of SEQ ID NO: 9 or 11 in claim 102; wherein said polypeptide comprises an amino acid sequence selected from the group consisting of (a) amino acids 58-342 of SEQ ID NO: 4, 6, 10, 12 or 31, (a) amino acids 58-404 of SEQ ID NO:4 or 6, (c) amino acids 74-342 of SEQ ID NO:4, 6, 10, 12 or 31, (d) amino acids 74-404 of SEQ ID NO:4 or 6, (e) amino acids 58 through 365 of SEQ ID NO:10, 12, or 31 and (f) amino acids 74-365 of SEQ ID NO:10, 12 or 31 in claim 105, wherein said polypeptide is produced by a process comprising culturing a recombinant host cell into which a polynucleotide comprising a nucleotide sequence encoding said polypeptide has been introduced in claim 111.

Applicant's arguments, filed 6/30/03, have been fully considered, but have not been found convincing.

Applicant argues that an adequate written description is achieved because (A) the members of the presently claimed genuses share a distinguishing partial structure: they comprise an amino acid sequence at least 80% identical to a portion of the nectin-3, (C) the members of the presently claimed genus share distinguishing functional characteristics, or (D) There is a known correlation between structure and function for members of each genus.

However, the Examiner notes that the claimed invention which is drawn to a genus may be adequately described if there is a (1) sufficient description of a representative number of species, or (2) by disclosure of relevant, identifying characteristics sufficient to describe the claimed invention in such full, clear, concise and exact terms that a skilled artisan would recognize applicant was in possession of the claimed invention. To satisfy the disclosure of a "representative number of species" will depend on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. "Relevant, identifying characteristics" include structure or other physical and /or chemical properties, functional characteristics coupled with a known or disclosed correlation between function and structure, or a combination of such identifying characteristics sufficient to show the applicant was in possession of the claimed genus. (see Revised Guidelines for the Examination of Patent

Applications Under the 35 U.S.C.112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No.4, pages 1099-1111, Friday January 5, 2001).

In the instant case, however, there is no described or art-recognized correlation or relationship between the structure of the invention, the nectin-3 extracellular domain, and it's inhibition of endothelial cell migration, the feature deemed essential to the instant invention. Therefore, one of skill in the art would not envisage, based on the instant disclosure, the claimed genus of polypeptides 'comprising' amino acids 58-404, 74-365, 58-342, 74-342, 74-404, 74-365 or 74-152, 189-250 and 287-342 or variants thereof, wherein the variant has at least 80%, 85%, 90%, 95% or 99% sequence identity of nectin-3 which retain the features essential to the instant invention.

12. No claim is allowed.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad, whose telephone number is (703) 306-3472. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 872-9307.

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600
September 30, 2003

Christina Chan
CHRISTINA CHAN
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